REMARKS/ARGUMENTS

Claims 1-13 and 17-20 are active.

Non-elected claims 5-13 have been retained for the purposes of expanding consideration and search to non-elected species.

Claims 17-20 find support in the specification at page 16-17.

The remaining amendments are for clarity with no new matter introduced.

The claim objections noted at page 3 of the Action are no longer applicable as Claims 14 and 16 have been cancelled.

Applicants thank Examiner Teller for the courtesy of meeting with their undersigned representative on May 29, 2008 to discuss the issues raised in the Official Action.

As explained during the meeting, contrary to the position laid out in the rejection under 112, first paragraph, the specification does provide adequate description to show possession of what is claimed.

Claim 1, for example, defines a compound "consisting of" that has at least 3 amino acids in the amino acid sequence SEQ ID NO:1, which is 17 amino acids in length. In other words, the compound is at most 17 amino acids in length with the amino acids defined in SEQ ID NO:1 and at minimum 3 amino acids in length AND having at least the Leu at position 11. The compound is also defined as having a N-terminal substitution and a hydroxyethylene group replacing the peptide bond between Leu-11 and the adjacent amino acid (Thr or Val).

The specification unquestionably describes the full 17 amino acid sequence and contrary to the statement on page 6 of the Action, both the claims and the specification define a conserved core, i.e. Leu-11-Val-12 or Thr-10-Leu-11 (with the defined peptide bond replaced with a hydroxyethylene group). SEQ ID NO:1 is in the sequence listing.

Further species within that definition are provided in SEQ ID NO:2 and SEQ ID NO:3.

One of ordinary skill would recognize and be able to envision a minimum of 3 amino acids within SEQ ID NO:1 up to the 17 amino acids defined in Claim 1.

Therefore, the claims meet the requirements of written description under 35 USC 112, first paragraph.

Withdrawal of the rejection is requested.

The discussion then turned to the rejection under 35 USC 103(a) based on the combination of the Yu publication and the Konvalinka publication.

It was explained that Yu does perform a characterization of the γ C-terminal fragment of APP generated by γ-secretase cleavage and identify amino acids that mediate the proteolytic reaction (see Discussion at page 43758, 2nd col., 2nd ¶). However, there is no suggestion in that Yu paper for the selection of a particular peptide region focusing on the ϵ-site of APP (as opposed to the γ-site) and that such modified peptides (as defined in the claims) inhibit γ-secretase and suppress production of amyloid protein.

Further, while Konvalinka does discuss the inclusion of hydroxethylene bonds neither Konvalinka nor Yu describe a modification at the N-terminus. Of course, Konvalinka does not describe APP protein nor fragments and therefore is not relevant to the aspect of selecting a particular peptide region focusing on the ϵ-site of APP.

These inhibitory effects are shown in the Examples. Example 3 determines Inhibitory Activity with the data shown in Tables 2 and 3:

Table 2

Compound's Inhibitory Activity -1

		DMSO			Inhibitor (100 μM)		
		Aβ42(43) (pg/ml)	Aβ40 (pg/ml)	Ratio of Aβ42(43)/ Aβ40	Aβ42(43) (pg/ml)	Aβ40 (pg/ml)	Ratio of Aβ42(43)/ Aβ40
1	Mock treatment	0	0	–	0	0	–
2	Wild-type APP695	1415	9656	0.147	415	218	1.90
3	London-type APP695	2845	6623	0.430	855	151	5.66
4	Sweden-type APP695	2503	17002	0.147	1311	1726	0.76

Table 3

Compound's Inhibitory Activity -2

		Inhibition rate (%)		
		Aβ42(43)	Aβ42	Total Aβ
1	Mock treatment	–	–	–
2	Wild-type APP695	71	98	98
3	London-type APP695	70	98	89
4	Sweden-type APP695	48	90	84

As evident from Tables 1 and 2, the inhibitor exhibited an inhibitory activities of about 71 % for Aβ42(43) production and nearly 100 %, i.e., about 98 % for Aβ40 production. About 98 % inhibition was achieved even on the total amyloid protein. (see page 26 of the specification).

Further in Example 4, to directly demonstrate that the inhibitory effect of the compound of the present invention is due to inhibition of γ-secretase (but not due to inhibition of β-secretase), an experiment was carried out in the same manner as in Example 3 except that an APP artificial fragment (referred to as C100), which lacked a polypeptide portion that is to be cut off in the first stage, was used instead of APP695, and amyloid protein thus produced was measured. The data and discussion of that data are reproduced below:

Table 4

Compound' Inhibitory Activity -3

		DMSO			Inhibitor (100 μM)			Inhibition rate (%)		
		Aβ42(43) (pg/ml)	Aβ40 (pg/ml)	Total Aβ (pg/ml)	Aβ42(43) (pg/ml)	Aβ40 (pg/ml)	Total Aβ	Aβ42(43)	Aβ40	Total Aβ
1	C100	127	944	1071	62	100	162	51	89	85

In the experiment using a C-100 APP (wild type), nearly the same inhibitory activity was observed as was in the Sweden-type mutation, i.e., about 90 % inhibition for Aβ40 and about 50 % inhibition for Aβ42(43). In each case where a familial disease-type mutation is present, more than about 80 % of inhibition was observed on total production of amyloid protein. Further inhibitory data in cell lines is provided in Example 6 (page 32 of the specification).

Thus, while Yu describes regions of APP that are cleaved and Konvalinka describes hydroxethylene bonds, the combination of art provides neither the direction to select the claimed peptides nor a reasonable prediction that such peptides would have the type of inhibitory activity as claimed.

Reconsideration and withdrawal of the rejection is requested.

Applicants request that the provisional rejection under the doctrine of obviousness type double patenting in view of co-pending application no. 11/664,714 be held in abeyance since the alleged conflicting claims have not yet been patented. Further, Applicants note the following from MPEP § 822.01:

> The "provisional" double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in one of the applications. If the "provisional" double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw that rejection and permit the application to issue as a patent, thereby converting the "provisional" double patenting

rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent.

There being no further issues, a Notice of Allowance is requested.

Respectfully submitted,

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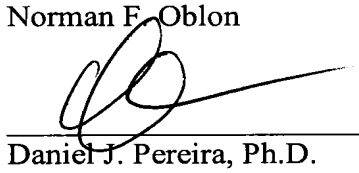

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